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SUBJECT OF INVESTIGATION

STUDIES ON IMMUNOLOGICAL  
DIAGNOSIS AND CHEMOTHERAPY  
OF PARAGONIMIASIS  
(LUNG FLUKE DISEASE)

RESPONSIBLE INVESTIGATOR

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Interim Report

Abstract report of the progress and phase of the work for one year from 18 April 1963 through 17 April 1964, and studied during the period from 18 April 1963 to 17 October 1963.

1. Comparison of the efficacies of Bitin-s-oxide with Bitin.

This study was designed to compare the efficacy of Bitin-s-oxide which was newly prepared as the derivative of Bitin with that of Bitin as follows;

No. of cases	drugs	daily dose	method of administration
9	Bitin	10 mg/kg	orally. every other day for 10 times
9	Bitin-s-oxide	10 mg/kg	"
7	Bitin	20 mg/kg	"
7	Bitin-s-oxide	20 mg/kg	"

The follow-up observations with stool examination, Complement-fixation test and Chest X-Ray examination were made at one month, 3 months, 6 months and 12 months after treatment.

The decision of complete cure was given to those cases in which no Paragonimus eggs were found in stools for more than 6 months after treatment.

Complete cure was observed in all of 9 cases receiving 10 mg/kg of Bitin-s-oxide but the one exception was found among 9 cases receiving 10 mg/kg of Bitin as shown in Table 1.

In the group given 20 mg/kg of Bitin-s-oxide a cure was observed in all of 7 cases and in the group given 20 mg/kg of Bitin a cure was also observed in all of 7 cases as shown in Table.

The changes of Antibody titers in Complement-fixation test were also shown in Table 1 and 2.

In the groups given 10 mg/kg of Bitin and Bitin-s-oxide, except one relapsed case, all of the cases showed the decrease of antibody titers in Complement-fixation test for 12 months after treatment. However, one case which showed no changes of antibody titer in Complement-fixation reaction for 6 months after treatment was found each in the groups given 20 mg/kg of Bitin and Bitin-s-oxide, although the examination for eggs showed negative results for 6 months after treatment.

Further observation are now being made.

Any significant difference in the frequency of side effects between Bitin and Bitin-s-oxide was not observed.

The changes of the abnormal shadows in the Chest X-Ray for 12 months after treatment were also shown in Table 3.

## 2. Epidemiological survey for paragonimiasis in Noto district of Ishikawa Prefecture, Japan.

The epidemiological survey for paragonimiasis using intradermal tests, Complement-fixation tests and stool examinations were conducted in Takahama-machi and Shika-machi, Noto district of Ishikawa Prefecture, Japan.

The results obtained in this survey are as follows:

In school children of Takahama-machi, 44(2,6 %) out of 1,722 showed positive or doubtful skin reactions. Among those 44 cases which showed positive or doubtful skin reactions, 13 cases were positive for complement-fixation tests and 4 cases were positive for Paragonimus eggs in stool as shown in Table 4.

In Shika-machi, 26(2,5 %) out of 1,023 inhabitants were positive or doubtful for intradermal reaction, and 4 of them were positive for complement-fixation tests as shown in Table 4.

Stool examination of those individuals who showed positive skin reaction are now under examination.

Table 1. Changes of dilution titer of Antiserum in Complement-fixation test on the individuals before and after treatment with daily dose of 10 mg/kg of Bitin and Bitin- $\alpha$ -oxide.

Case No.	Name	Age	Sex	Before treatment	During treatment	Immediately after treatment		After treatment			
						1M.	3M.	6M.	12M.		
(Bitin)											
1. S.S.	9	F		>X160 (38)		X160 (0)	>X160 (0)	X100 (0)	X 31 (0)	X 14 (0)	
2. H.M.	11	M		X 25 (8)	X 20 (0)	(0)	(0)	(0)	(0)	(0)	
3. H.A.	13	M		>X160 (95)	(0)	>X160 (0)	>X160 (0)	X 87 (0)	X 27 (0)	X 13 (0)	
4. K.O.	14	M		X 67 (47)	X 51 (0)	X 67 (0)	X 66 (0)	X 12 (0)	(0)	(0)	
5. Y.M.	14	M		X 33 (14)	X 26 (0)	X 24 (0)	(0)	X 17 (0)	(0)	(0)	
6. H.K.	13	M		X160 (4)	X110 (0)	X115 (0)	X 66 (0)	X 40 (0)	X 20 (0)	X 18 (0)	
7. T.T.	64	F		>X160 (13)	>X160 (0)	>X160 (0)	>X160 (0)	X110 (0)	X 51 (0)	X 40 (0)	
8. S.T.	19	M		>X160 (11)	X120 (0)	X146 (0)	(0)	X 64 (0)	X 32 (0)		
9. T.S.	22	M		X 76 (4)	X 40 (2)	X 31 (0)	(0)	X 48 (8)	X 49 (6)	X 17 (0)	
(Bitin- $\alpha$ -oxide)											
10. S.M.	12	F		>X160 (216)	>X160 (106)	X160 (0)	>X160 (0)	X160 (0)	X 53 (0)	X 21 (0)	
11. T.I.	13	M		X 55 (18)	X 57 (0)	X 57 (0)	X 95 (0)	X 36 (0)	X 20 (0)	(0)	
12. S.M.	13	M		X 44 (17)	X 40 (1)	X 22 (0)	X 14 (0)	X 15 (0)	(0)	(0)	
13. O.N.	13	M		X 53 (10)	X 44 (1)	X 33 (0)	X 69 (0)	X 15 (0)	X 13 (0)		
14. K.I.	14	F		X 80 (39)	(2)	X 80 (0)	X 70 (0)	X 52 (0)	X 18 (0)		
15. S.Y.	16	M		X 25 (2)	X 24 (0)	X 11 (0)	X 17 (0)	X 17 (0)	(0)	(0)	
16. K.Y.	24	M		>X160 (49)	(0)	>X160 (0)	(0)	X 67 (0)	X 13 (0)	X 15 (0)	
17. M.S.	15	M		X 58 (11)	X 47 (0)	X 72 (0)	X 56 (0)	X 58 (0)	X 13 (0)	X 12 (0)	
18. T.H.	21	M		>X160 (17)	(0)	>X160 (0)	(0)	X 47 (0)	(0)	(0)	

( ) -- Number of eggs per gram in stools.

Table 2. Changes of dilution titer of Antiserum in Complement-fixation test on the individuals before and after treatment with daily dose of 20 mg/kg of Bitin and Bitin-s-oxide.

Case No.	Name	Age	Sex	Before treatment	During treatment	Immediately after treatment	1M.	3M.	6M.
<b>(Bitin)</b>									
1. S.K.	54	F		X122 (18)	X 76 (0)	X 40 (0)	X 26 (0)	X 30 (0)	- (0)
2. H.A.	67	M		>X160 (4)	>X160 (0)	>X160 (0)	>X160 (0)		X 56 (0)
3. M.Y.	53	M		X 20 (6)		X 20 (0)	- (0)	- (0)	- (0)
4. T.O.	15	F		X 25 (24)	X 40 (0)	X 63 (0)	-	X 15 (0)	
5. T.T.	50	F		X 48 (16)	X 57 (0)	X118 (0)		X 61 (0)	
6. H.E.	15	M.		X 15 (2)		X 10 (0)	- (0)	- (0)	- (0)
7. H.K.	52	M		X 37 (2)			X 27 (0)	X 20 (0)	- (0)
<b>(Bitin-s-oxide)</b>									
8. H.W.	52	M		>X160 (8)	>X160 (0)	X105 (0)	X 56 (0)	X 27 (0)	- (0)
9. Z.E.	52	M		>X160 (20)	X 48 (0)	X 53 (0)	X 20 (0)	X 22 (0)	- (0)
10. S.S.	55	M.		>X160 (2)	X129 (0)	X 57 (0)	X 17 (0)	X 27 (0)	- (0)
11. Y.S.	14	F		X156 (10)	X 56 (31)	X 50 (0)	-	-	- (0)
12. S.K.	68	M		X128 (6)	X 60 (0)	X107 (0)	X 56 (0)	X 53 (0)	X 58 (0)
13. K.M.	56	F		>X160 (24)	>X160 (0)	>X160 (0)	>X160 (0)	>X160 (0)	>X160 (0)
14. S.M.	17	F		X 11 (6)	(0)	(0)	- (0)	(0)	- (0)

( ) --- Number of eggs per gram in stools.

Table 3. The follow-up studies on the Chest X-ray findings of the patients treated with daily dose of 10 mg/kg of Bitin and Bitin-s-oxide.

Case No.	Name	Age	Sex	Before treatment		Immediately after treatment		After treatment			
								1M.	3M.	6M.	12M.
(Bitin)											
1. S.S.	9	F		1-diffused infiltrative shadow	unchanged	reduced	reduced	reduced	reduced	reduced	reduced
2. M.M.	11	M		r-diffused infiltrative shadow	unchanged	reduced	reduced	disappeared	..	..	..
3. H.A.	13	M		both-diffused infiltrative shadow	reduced	reduced	reduced	reduced	disappeared	..	..
5. Y.M.	14	M		r-diffused infiltrative shadow	reduced	reduced	disappeared	-	-	-	-
6. H.K.	13	M		r-strand shadow	unchanged	unchanged	unchanged	unchanged	unchanged	unchanged	unchanged
7. T.T.	64	F		r-diffused infiltrative shadow	unchanged	unchanged	reduced	reduced	reduced	reduced	reduced
8. S.T.	19	M		1-diffused infiltrative shadow	unchanged	reduced	reduced	reduced	reduced	reduced	reduced
9. P.S.	22	M		r-ring shadow r-diffused infiltrative shadow	unchanged unchanged	reduced reduced	unchanged unchanged	reduced unchanged	reduced unchanged	unchanged	unchanged
(Bitin-s-oxide)											
10. S.M.	12	F		l-ring shadow 1-diffused infiltrative shadow	reduced reduced	disappeared	-	-	-	-	-
12. S.M.	13	M		r-diffused infiltrative shadow	reduced	reduced	disappeared	-	-	-	-
13. C.N.	13	M		both-diffused infiltrative shadow	reduced	reduced	disappeared	-	-	-	-
14. J.I.	14	F		r-diffused infiltrative shadow	reduced	reduced	reduced	reduced	reduced	reduced	reduced
16. K.Y.	24	M		r-diffused infiltrative shadow	unchanged	disappeared	-	-	-	-	-
17. A.S.	13	M		1-diffused infiltrative shadow	unchanged	reduced	disappeared	..	..	-	-

Table 4. Results of Intradermal test, Complement-fixation test and Stool examination.

Location	Object	No. examined	Intradermal test (+)	Intradermal test (±)	Total	C.F.-test (+)	Eggs (+)
Takahama machi	Primary school children	704	9	10	19(2.7%)	3/19	1/19
	Middle school children	1,018	20	5	25(2.5%)	10/25	3/25
	Total	1,722	29	15	44(2.6%)	13/44 (29.5%)	4/44 (9.1%)
Shika machi	Inhabitants	1,023	18	8	26(2.5%)	4/26 (15.4%)	